No. 93

THE ACTION OF NITRIC ACID ON THE ETHERS OF AROMATIC HYDROXYALDEHYDES

BY

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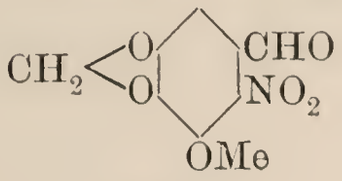
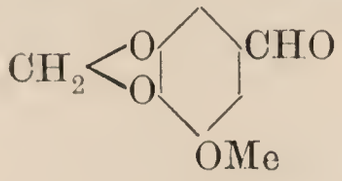
CXXX.—*The Action of Nitric Acid on the Ethers of Aromatic Hydroxyaldehydes.*

By Arthur Henry Salway.

In the course of some experiments on the synthesis of substances allied to cotarnine, the author had occasion to prepare a compound of the formula (I), and an attempt was made to achieve this object by



(I.)



(II.)

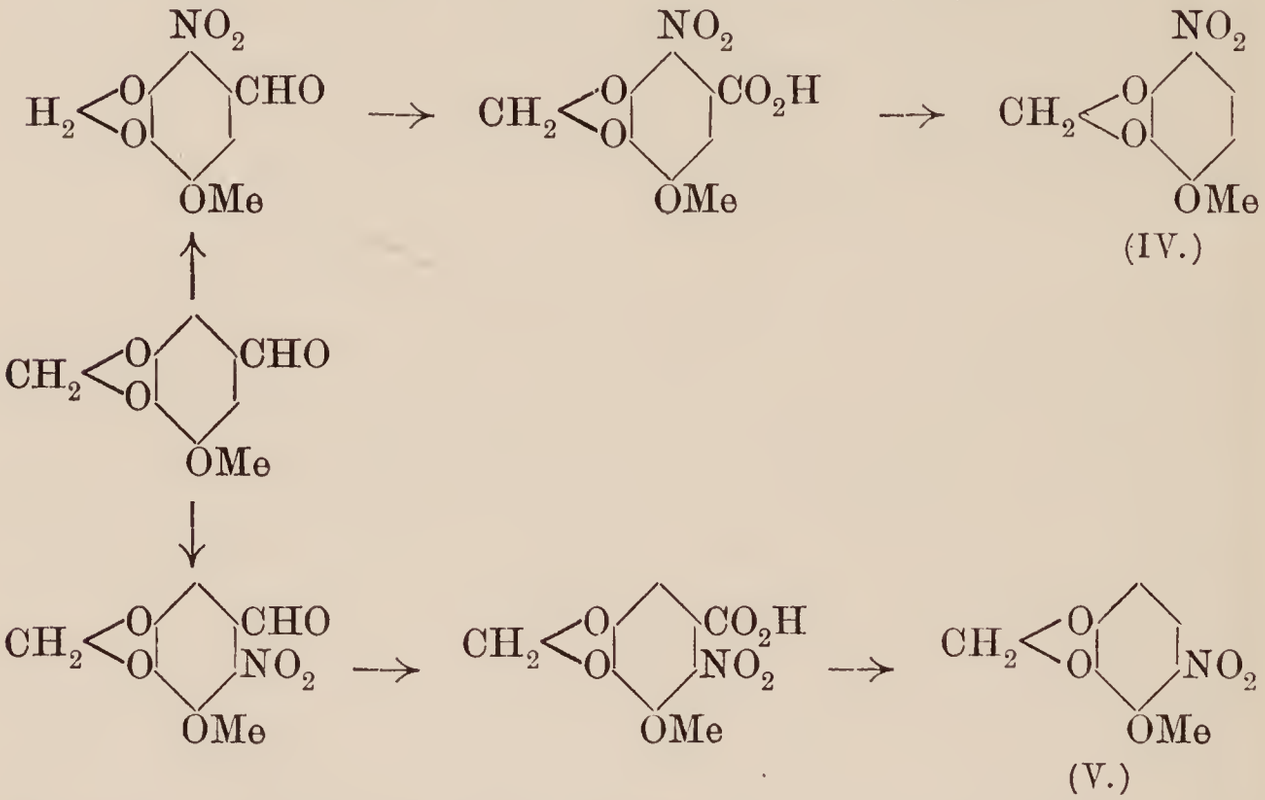
the action of nitric acid on myristicinaldehyde (II). The yield of the desired nitroaldehyde was comparatively small, the principal product of the reaction being a neutral nitro-compound, which did not contain an aldehyde group, and was found to consist of a nitromethoxymethylenedioxybenzene. The formation of the latter compound from myristicinaldehyde is evidently due to the elimination of the aldehyde group and the introduction of a nitro-group into the nucleus.

It will be seen that the orientation of the nitro-group in this nitromethoxymethylenedioxybenzene is essential for the correct interpretation of the manner in which the aldehyde group is eliminated. Thus it might be supposed, on the one hand, that the aldehyde group undergoes direct substitution by a nitro-group, in which case the constitution of the resulting nitro-compound would be represented by formula (III); on the other hand, it is conceivable that the myristicinaldehyde primarily undergoes nitration with the formation of nitromyristicinaldehyde, which, by oxidation to the corresponding nitrocarboxylic acid and subsequent liberation of carbon dioxide, becomes converted into a nitromethoxymethylenedioxybenzene. In this case the constitution of the latter would be represented by (IV) or (V).

The formation of nitromyristicinaldehyde as one of the products of the nitration of myristicinaldehyde lends some degree of probability to the latter view. However, on further oxidising nitromyristicinaldehyde, the only product was the stable nitromyristicinic acid, and there was no evidence of the formation of nitromethoxymethylenedioxybenzene. It appeared, therefore, improbable that this compound owes its formation to the intermediate production of nitromyristicinaldehyde according to (IV) or (V), and it was subsequently proved beyond question by the following series of reactions that nitromethoxymethylenedioxybenzene is produced by the direct substitution of the aldehyde group according to (III).

Myristicinaldehyde was converted, on the one hand, by means of nitric acid into nitromethoxymethylenedioxybenzene—the constitution of which was to be determined—and the latter reduced to the corresponding amino-derivative; on the other hand, myristicinaldehyde was

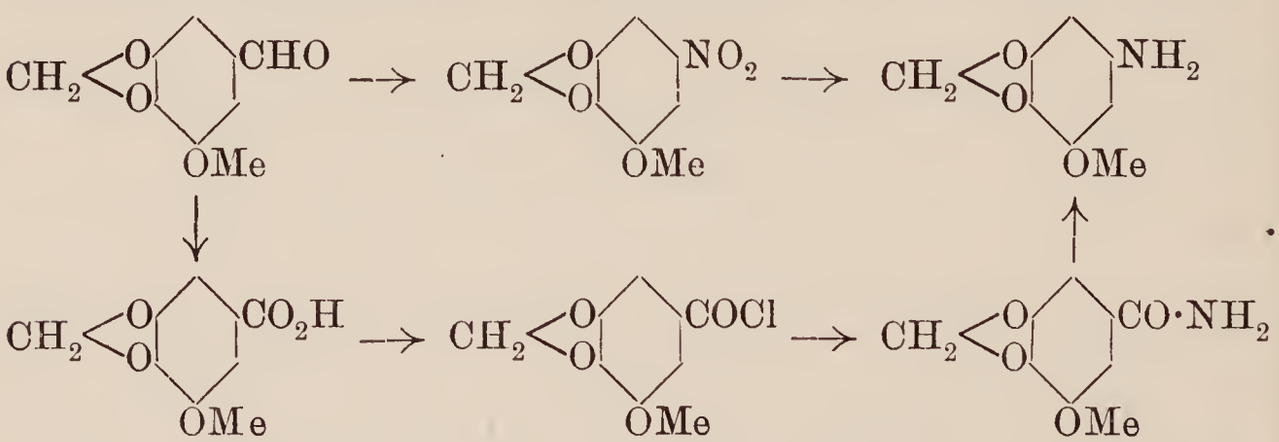
(III.)



(IV.)

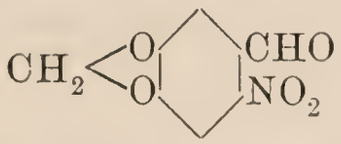
(V.)

oxidised to myristicinic acid, which, after successive transformation into the chloride and amide, was finally converted into 5-amino-1-methoxy-2 : 3-methylenedioxybenzene, the constitution of which follows from that of myristicinaldehyde. The amines obtained in these two series of reactions were identical and gave identical derivatives :



It next seemed of interest to ascertain whether the displacement of the aldehyde group by a nitro-group is a reaction common to the alkyl ethers of aromatic hydroxyaldehydes. Piperonal (Fittig and Remsen, *Annalen*, 1871, **159**, 34), vanillin methyl ether (Pschorr and Sumuleanu, *Ber.*, 1899, **32**, 3405), and anisaldehyde (Einhorn and

Grabfield, *Annalen*, 1888, **243**, 370) have already been subjected by the above-mentioned investigators to the action of concentrated nitric acid; in each case the corresponding nitroaldehydes were obtained, but the formation of nitroalkyloxybenzenes was not observed. On repeating these experiments it was found, however, that both piperonal and vanillin methyl ether exhibit the same behaviour towards nitric acid as myristicinaldehyde, that is to say, part of the aldehyde is directly nitrated, whilst the remainder undergoes nitration with elimination of the aldehydic group. Thus piperonal is converted by nitric acid at 0° into a mixture of nitropiperonal and 4-nitro-1 : 2-methylenedioxybenzene :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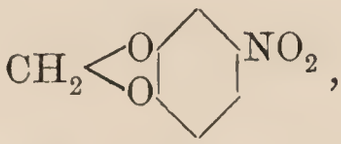
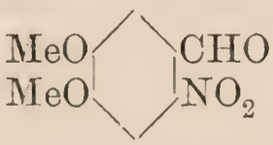
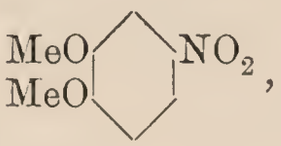
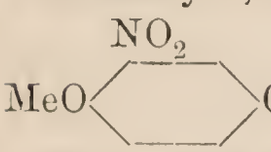


the separation of which was easily effected by means of sodium hydrogen sulphite. Vanillin methyl ether, under similar conditions yielded a mixture of nitrovanillin methyl ether and 4-nitroveratrole :


and


Anisaldehyde, on the other hand, was converted into nitroanisaldehyde,



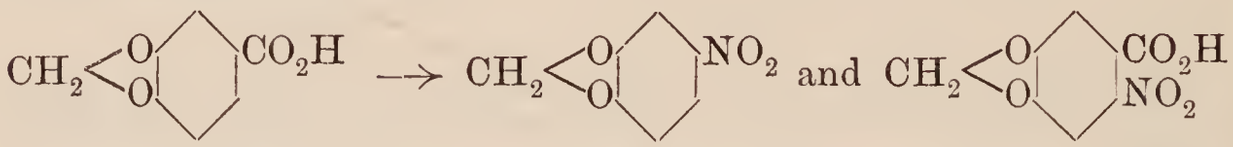
without the formation of any *p*-nitroanisole.

The results of the above experiments on the nitration of the alkyl ethers of aromatic hydroxyaldehydes also serve to elucidate the hitherto unexplained observations of Ginsberg (*Ber.*, 1888, **21**, 108) respecting the action of nitric acid on apiolaldehyde. In this case a nitro-compound melting at 116° was obtained, to which no formula could be assigned. With consideration of the analytical data recorded by Ginsberg in connexion with this nitro-compound and its derivatives, it is now evident that the substance melting at 116° is dinitroapione, and that it was formed from apiolaldehyde by removal of the aldehyde group with simultaneous nitration:

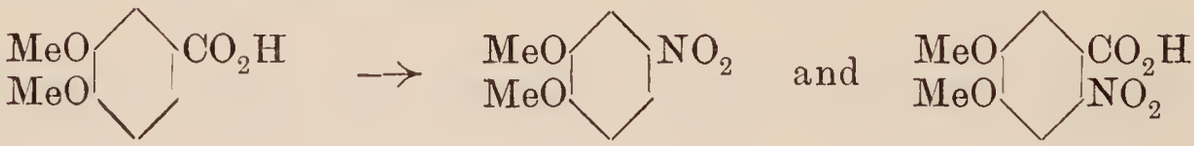
It is worthy of note that with the accumulation of alkyloxy-groups the elimination of the aldehyde group on nitration takes place with greater readiness, and that the formation of the nitroalkyloxy-benzaldehyde is inhibited in a corresponding degree. Thus the formation of 5-nitro-1-methoxy-2 : 3-methylenedioxybenzene from

myristicinaldehyde takes place to the extent of 60·6 per cent. Piperonal, on the other hand, yields only 30 per cent. of 4-nitro-1 : 2-methylenedioxybenzene, whilst with anisaldehyde substitution of the aldehydic group does not occur.

Although the direct displacement of the aldehydic group of the ethers of aromatic hydroxyaldehydes by the nitro-group has not hitherto been observed, an analogous transformation, in which the carboxyl group of the corresponding ethers of aromatic hydroxy-acids is eliminated with simultaneous nitration, has long been on record. Thus Jobst and Hesse (*Annalen*, 1879, **199**, 70) have shown that when piperonylic acid is acted on by concentrated nitric acid, it is converted into a mixture of 4-nitro-1 : 2-methylenedioxybenzene and nitropiperonylic acid :

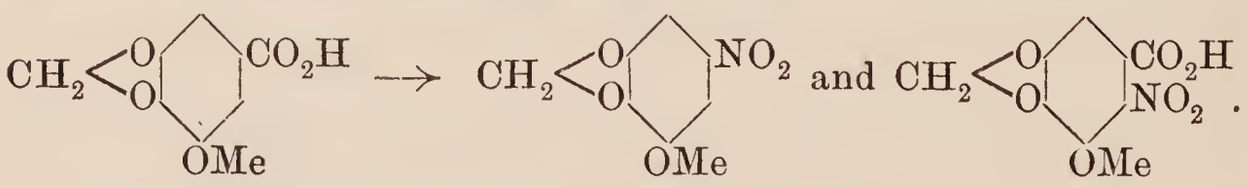


A similar reaction has been observed by Tiemann (*Ber.*, 1876, **9**, 936) in the case of veratric acid, which yields on nitration 4-nitroveratrole and nitroveratric acid:

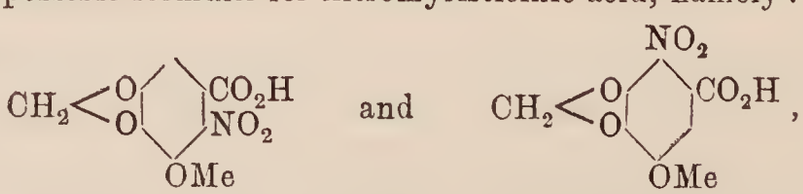


Furthermore, Weselsky and Benedikt (*Ber.*, 1892, **25**, 722) have shown that the triethyl ether of gallic acid is almost quantitatively converted by nitric acid into 5-nitropyrogallol triethyl ether :

In addition to these observations, the present author has investigated the action of nitric acid on myristicinic acid, and has found that a similar reaction ensues with the formation of a mixture of 5-nitro-1-methoxy-2 : 3-methylenedioxybenzene and nitromyristicinic acid :*

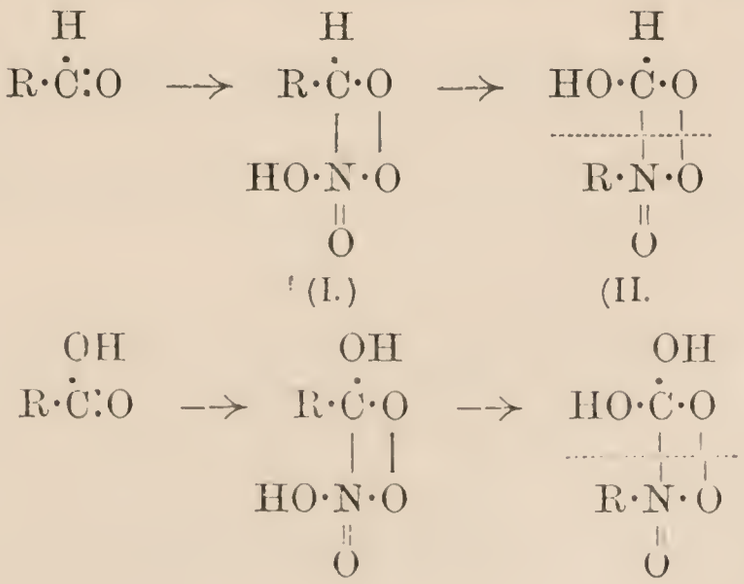


* Of the two possible formulæ for nitromyristicinic acid, namely :



the former has been adopted throughout this communication, and the same applies in the case of nitromyristicinaldehyde.

In consideration of the fact that the ethers of aromatic hydroxyaldehydes, under the influence of nitric acid, show the same transformation as the corresponding carboxylic acids, it might at first be supposed that the reaction in the case of the former depended primarily on their oxidation to the latter. That this view, however, is untenable is evident from the following considerations based on experiments with myristicinaldehyde and myristicinic acid. When myristicinic acid is acted on by nitric acid in the cold, the chief product is 5-nitro-1-methoxy-2 : 3-methylenedioxybenzene, but some nitromyristicinic acid is always formed. If, therefore, myristicinic acid is an intermediate product in the action of nitric acid on myristicinaldehyde, nitromyristicinic acid would be formed in this reaction. As a matter of fact, however, no acid whatsoever is produced. For this reason it would seem that the carbonyl group, which is common to both series of compounds, is alone responsible for the reaction, and that any explanation of the mechanism of the transformation must be sought for in the action of nitric acid on this group. Although there is at present no direct evidence on which the mechanism of the reaction may be based, the following explanation may be suggested. In the first place it is conceivable that the carbonyl of the aldehyde group forms with nitric acid an additive product (I), which subsequently undergoes a change analogous to the Beckmann transformation. The resulting substance (II) is, however, unstable, and decomposes, as indicated by the dotted line below, with the formation of a substituted nitrobenzene and formic acid, the latter in the presence of nitric acid being oxidised to carbon dioxide.



Experimental.

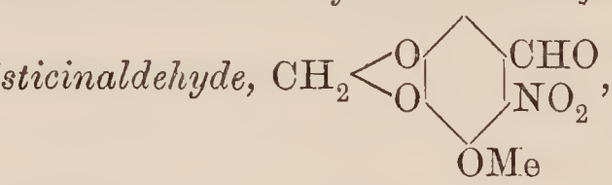
Action of Concentrated Nitric Acid on Myristicinaldehyde.

One part of finely divided myristicinaldehyde was added in small quantities at a time to 7 parts of nitric acid (sp. gr. 1·42) at 0°. The

myristicinaldehyde gradually passed into solution, and after a short time carbon dioxide was slowly evolved. The mixture was kept at 0° for an hour, then poured into ice-water, and the yellow precipitate collected and washed free from nitric acid. It was then shaken with an excess of aqueous sodium hydrogen sulphite, by means of which a separation into a soluble and an insoluble portion was effected. The soluble portion was reprecipitated by adding dilute aqueous sodium hydroxide, collected, and washed. The yield of this substance amounted to 39·4 per cent. of the myristicinaldehyde employed. It was crystallised from alcohol, and was obtained in well-formed, prismatic needles, melting at 131—132°:

0·1134 gave 0·2000 CO_2 and 0·0360 H_2O. C = 48·1; H = 3·5.
$C_9H_7O_6N$ requires C = 48·0; H = 3·1 per cent.

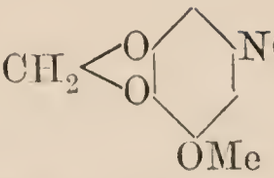
The analysis and chemical behaviour of this compound show that it is a mononitro-derivative of myristicinaldehyde.

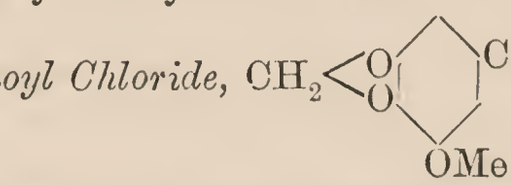
Nitromyristicinaldehyde,  , is easily soluble in the usual organic solvents with the exception of light petroleum. It is readily soluble in aqueous sodium hydrogen sulphite, giving a deep yellow solution. When freshly crystallised from alcohol it is practically colourless, but on exposure to light quickly becomes deep yellow. When oxidised with alkaline permanganate it is converted into nitromyristicinic acid, which melts and decomposes at 245°, and is identical with the acid obtained by the nitration of myristicinic acid (p. 1165).

The portion of the product of the action of nitric acid on myristicinaldehyde which was insoluble in sodium hydrogen sulphite amounted to 60·6 per cent. of the aldehyde employed. It was purified by crystallisation from alcohol, from which it separated in long, almost colourless needles, melting at 143—144°:

0·1386 gave 0·2481 CO_2 and 0·0481 H_2O. C = 48·8; H = 3·9.
0·2928 „ 17·5 c.c. N_2 at 20° and 766 mm.. N = 6·9.
$C_8H_7O_5N$ requires C = 48·7; H = 3·6; N = 7·1 per cent.

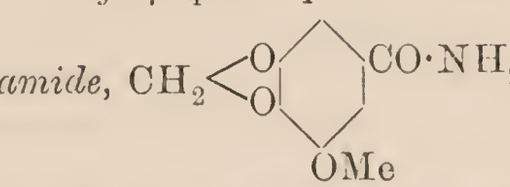
It is evident that the formation of a compound, $C_8H_7O_5N$, from myristicinaldehyde could only be brought about by the elimination of the aldehydic group and simultaneous introduction of a nitro-group into the molecule. The substance melting at 143—144° must be, therefore, a nitromethoxymethylenedioxybenzene. As explained in the introduction, of the three possible nitro-1-methoxy-2 : 3-methylenedioxybenzenes, the present one must contain the nitro-group in the 5-position.

5-Nitro-1-methoxy-2 : 3-methylenedioxybenzene,  , is readily soluble in alcohol, ethyl acetate, or benzene, from each of which it crystallises in long, almost colourless needles. It may readily be sublimed when heated above its melting point. When warmed with alcoholic potash it is hydrolysed to the corresponding nitrophenol, *5-nitro-1-hydroxy-2 : 3-methylenedioxybenzene*, which crystallises from water in yellow, silky needles melting at 94°, and is soluble in alkalis with a deep red colour. In determining the constitution of 5-nitro-1-methoxy-2 : 3-methylenedioxybenzene it was necessary, as already explained, to prepare successively myristicinoyl chloride, myristicinamide, and 5-amino-1-methoxy-2 : 3-methylenedioxybenzene. Since these substances have not hitherto been described, the method of preparation, together with their characteristic properties, may briefly be indicated.

Myristicinoyl Chloride,  .—A mixture of myristicinic acid (1 mol.) and phosphorus pentachloride (1 mol.) was heated for a short time at 100°. After removal of the phosphoryl chloride, the product was purified by distillation under diminished pressure. *Myristicinoyl chloride* distils at 189—190°/20 mm. as a colourless oil, which rapidly solidifies, and crystallises from a mixture of benzene and light petroleum in long, thin, colourless needles melting at 105° :

0·3236 gave 0·2200 AgCl. Cl = 16·8.

$C_9H_7O_4Cl$ requires Cl = 16·6 per cent.

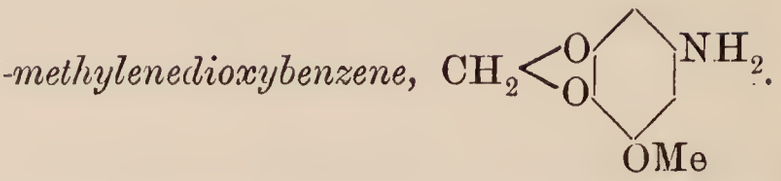
Myristicinamide,  .—To a solution of myristicinoyl chloride in benzene an excess of concentrated ammonia was added, and the mixture vigorously shaken. The precipitated amide was collected, and recrystallised from hot water, in which it is only moderately soluble. It separated in long, thin needles, which contain one molecule of water of crystallisation, and melts at 184°. It is readily soluble in hot alcohol, from which it is deposited in clusters of feathery needles :

0·7164 lost, at 105°, 0·0631 H_2O. H_2O = 8·8.

0·1485 gave 0·3028 CO_2 and 0·0660 H_2O. C = 55·6 ; H = 4·9.

$C_9H_9O_4N,H_2O$ requires H_2O = 8·5 per cent.

$C_9H_9O_4N$ requires C = 55·4 ; H = 4·6 per cent.

5-*Amino*-1-*methoxy*-2 : 3-*methylenedioxybenzene*,  .

(*a*) *Preparation from Myristicinamide.*—Finely powdered myristicinamide was shaken continuously for several hours with the theoretical quantity of a freshly-prepared solution of sodium hypochlorite (compare Graebe, *Ber.*, 1902, **35**, 2753), and the mixture finally heated at 100° for a short time. The product was then cooled and extracted with ether, when the ethereal solution, after evaporation, yielded an oily residue, which soon solidified. It was purified by crystallisation from water, from which it separated in colourless leaflets, melting at 85—86° :

0·1076 gave 0·2263 CO_2 and 0·0553 H_2O. C = 57·4 ; H = 5·7.

$C_8H_9O_3N$ requires C = 57·5 ; H = 5·4.

(*b*) *Preparation from* 5-*Nitro*-1-*methoxy*-2 : 3-*methylenedioxybenzene.*—To 1 part of the finely divided nitro-compound 5 parts of stannous chloride in 15 parts of concentrated hydrochloric acid were added, and the mixture was gently warmed for one hour. A crystalline tin double salt of the amino-compound was formed, from which the tin was removed by means of hydrogen sulphide. The aqueous solution was then concentrated to a small bulk, rendered alkaline with sodium carbonate, and extracted with ether ; the ethereal solution, after evaporation, left a residue which rapidly solidified and was crystallised from hot water, when it was deposited in colourless leaflets melting at 85—86°. When this substance was mixed with the 5-amino-1-methoxy-2 : 3-methylenedioxybenzene, prepared from myristicinamide as above described, the melting point remained unchanged. Further confirmation of the identity of the two products was obtained by the preparation from each of the same benzoyl derivative, melting at 128—129°.

5-*Amino*-1-*methoxy*-2 : 3-*methylenedioxybenzene* is readily soluble in benzene, ether, chloroform, ethyl acetate, or alcohol, but only sparingly soluble in light petroleum. It is best crystallised from hot water, but can also be crystallised from a mixture of benzene or alcohol and petroleum. Its *hydrochloride* crystallises from dilute alcohol in well-formed, colourless needles, which decompose at about 245°. It yields a *benzoyl* derivative, which crystallises from alcohol in colourless rosettes of feathery needles melting at 128—129° :

0·1136 gave 0·2770 CO_2 and 0·0506 H_2O. C = 66·5 ; H = 4·9.

$C_{15}H_{13}O_4N$ requires C = 66·4 ; H = 4·8 per cent.

Formation of 4-*Nitro*-1 : 2-*methylenedioxybenzene by the Action of Nitric Acid on Piperonal.*

The action of nitric acid on piperonal was first investigated by Fittig and Remsen (*Annalen*, 1871, **159**, 134), who isolated only nitropiperonal from the product of the reaction. This experiment has been repeated in order to ascertain whether, in addition to the formation of nitropiperonal, any portion of the piperonal is converted into 4-nitro-1 : 2-methylenedioxybenzene by elimination of the aldehydic group :

For this purpose 5 grams of finely divided piperonal were added in small quantities at a time to 50 c.c. of nitric acid (sp. gr. 1·41) at 0°. Each addition of piperonal immediately conglomerated to a solid cake, which was broken up by means of a glass rod. After all the piperonal had been added, the mixture was well shaken from time to time until complete solution was effected, for which about an hour was necessary. The mixture was then poured into ice-water, the yellow precipitate collected, washed free from nitric acid, and then shaken with a solution of sodium hydrogen sulphite. In this manner the product was separated into a soluble aldehydic portion and an insoluble neutral portion. The soluble portion was reprecipitated by adding alkali hydroxide, when it amounted to 3·6 grams, corresponding with a yield of 70 per cent. When crystallised from a mixture of alcohol and ethyl acetate, it was obtained in stout, yellow needles melting at 98°. This was identical with the nitropiperonal (m. p. 95·5°) described by Fittig and Remsen (*loc. cit.*). The portion insoluble in sodium hydrogen sulphite amounted to 1·5 grams, representing a yield of 30 per cent. When crystallised from hot alcohol it separated in long, yellow needles melting at 145°, and this melting point was not changed on recrystallisation :

0·2241 gave 16·1 c.c. N_2 at 16·5° and 767 mm.. N = 8·5.

$C_7H_5O_4N$ requires N = 8·4 per cent.

This substance is therefore identical with the 4-nitro-1 : 2-methylenedioxybenzene (m. p. 148°) described by Jobst and Hesse (*Annalen*, 1879, **199**, 70).

Formation of 4-*Nitroveratrole by the Action of Nitric Acid on Vanillin Methyl Ether.*

Five grams of vanillin methyl ether were gradually added to 50 c.c. of nitric acid (sp. gr. 1·41) at 0°. After one hour the mixture was

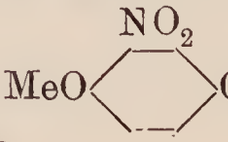
poured into cold water, the voluminous, yellow precipitate collected, washed with water, and shaken with a solution of sodium hydrogen sulphite. The soluble substance amounted to 94 per cent. of the aldehyde employed. When crystallised from alcohol it separated in yellow needles melting at 134°, and was identical with the nitrovanillin methyl ether of Pschorr and Sumuleanu (*Ber.*, 1899, **32**, 3405). The portion insoluble in sodium hydrogen sulphite amounted to 6 per cent. of the weight of the aldehyde employed. It crystallised from alcohol in stout, deep yellow needles, melting at 96°:

0·2548 gave 16·7 c.c. N_2 at 17° and 759 mm. N = 7·6.

$C_8H_9O_4N$ requires N = 7·7 per cent.

This substance is evidently 4-nitroveratrole (Tiemann, *Ber.*, 1876, **9**, 939; 1878, **11**, 131), and its formation is due to the direct displacement of the aldehydic group of vanillin methyl ether by a nitro-group:

Action of Nitric Acid on Anisaldehyde.

When anisaldehyde is treated with nitric acid at 0° under the same conditions as those described in connexion with the nitration of myristicinaldehyde, piperonal, etc., it first dissolves, and then immediately crystallises unchanged in long, colourless needles, which are only slowly attacked by the nitric acid. At the ordinary temperature, however, nitration takes place with greater readiness. The reaction was therefore conducted as follows: 5 grams of anisaldehyde were added, drop by drop, to 50 c.c. of concentrated nitric acid (sp. gr. 1·41) at the ordinary temperature; after about four hours, water was added, and the precipitated oil extracted with ether. The ethereal solution was first shaken with aqueous sodium hydrogen sulphite until free from aldehyde, then with dilute sodium carbonate, which removed a small quantity of anisic acid, and finally washed with a little water. After drying and removing the ether, no trace of *p*-nitroanisole was obtained. The aldehydic group of anisaldehyde is therefore not eliminated by the action of nitric acid in the cold. The portion of the product which had been extracted with sodium hydrogen sulphite was precipitated as a yellow solid by the addition of sodium hydroxide. This was collected, washed, and crystallised from alcohol, when long, colourless needles melting at 84° were obtained. It was identified as mononitroanisaldehyde,  , by conversion into its hydrazone melting at 132°;

0·0513 gave 0·1170 CO_2 and 0·0240 H_2O. C = 62·2 ; H = 5·2.

$C_{14}H_{13}O_3N_3$ requires C = 62·0 ; H = 4·8 per cent.

Einhorn and Grabfield (*Annalen*, 1888, **243**, 370), who first prepared mononitroanisaldehyde, assign to it a melting point of 83·5°, whilst, according to Wörner (*Ber.*, 1896, **29**, 157), it melts at 72°, and dinitroanisaldehyde at 86°. The above results confirm Einhorn and Grabfield's observation, and indicate that the correct melting point of nitroanisaldehyde is 84°.

The Action of Nitric Acid on Myristicinic Acid.

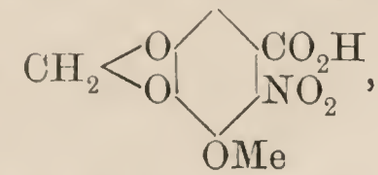
Twenty grams of myristicinic acid were gradually stirred into 300 c.c. of nitric acid (sp. gr. 1·41) at 0°. After a short time there was a vigorous evolution of carbon dioxide. The mixture was kept cold for an hour, then poured into ice-water, and the resulting precipitate collected and washed. By shaking with an aqueous solution of sodium carbonate, the product of the reaction was separated into a neutral and an acidic portion. The neutral portion amounted to 11·5 grams, corresponding to a yield of 57·5 per cent. It was crystallised from alcohol, when it was obtained in long needles melting at 143—144°. The substance was identical with the 5-nitro-1-methoxy-2 : 3-methylenedioxybenzene previously obtained by the nitration of myristicinaldehyde. The portion soluble in sodium carbonate was reprecipitated by the addition of dilute sulphuric acid, collected, and washed, when it amounted to 6·5 grams, representing a yield of 33·5 per cent. On recrystallisation from glacial acetic acid, it was deposited in radiating clusters of light yellow needles, which melted and decomposed at about 245° :

0·1667 gave 0·2746 CO_2 and 0·0450 H_2O. C = 44·9 ; H = 3·0.

0·2780 required 11·55 N/10-KOH for neutralisation. M.W. = 240·7

$C_9H_7O_7N$ requires C = 44·8 ; H = 2·9 per cent. M.W. = 241.

This substance is evidently a mononitromyristicinic acid.

Nitromyristicinic acid,  , is readily soluble in alcohol, ethyl acetate, or glacial acetic acid, but only sparingly so in benzene, chloroform, or hot water. From the latter it crystallises in colourless, silky needles, which slowly become yellow on exposure to light.

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